

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

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| Applicant's or agent's file reference 20363 - 025 - 061 | FOR FURTHER ACTION <div style="text-align: right; font-size: small;">see Form PCT/ISA/220 as well as, where applicable, item 5 below.</div> | |
| International application No. PCT/US2005/005922 | International filing date (<i>day/month/year</i>) 25/02/2005 | (Earliest) Priority Date (<i>day/month/year</i>) 25/02/2004 |
| Applicant DANA FARBER CANCER INSTITUTE, INC. | | |

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 09 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box II).

3. ☒ **Unity of invention is lacking** (see Box III).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

INHIBITORS OF INSULIN-LIKE GROWTH FACTOR RECEPTOR-1 FOR INHIBITING TUMOUR CELL GROWTH

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

a. the figure of the **drawings** to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☒ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2005/005922

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K45/06 A61K31/519 A61K39/395 A61K38/10 A61P35/00
A61K48/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, MEDLINE, WPI Data, PAJ, COMPENDEX, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| X | WO 02/092599 A (NOVARTIS AG; NOVARTIS-ERFINDUNGEN VERWALTUNGSGESELLSCHAFT M.B.H; CAPRA) 21 November 2002 (2002-11-21) cited in the application page 1, line 2 - line 24 page 33, line 17 - page 38, line 12 ----- | 1-17 |
| X | WO 02/102804 A (KAROLINSKA INNOVATIONS AB; LARSSON, OLLE; AXELSON, MAGNUS; AXELAR AB) 27 December 2002 (2002-12-27) abstract page 11, line 4 - line 10 ----- -/-- | 1-17 |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

18 May 2005

Date of mailing of the international search report

25. 08. 2005

Name and mailing address of the ISA

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Authorized officer

Pilling, S

| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|--|---|-----------------------|
| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | WO 03/027246 A (NOVO NORDISK A/S; DGI BIOTECHNOLOGIES; PILLUTLA, RENUKA; DEDOVA, OLGA;) 3 April 2003 (2003-04-03) page 97, line 21 - page 98, line 7 page 5, line 5 - line 9 ----- | 1-17 |
| X | WO 98/06391 A (MOR-RESEARCH APPLICATIONS LTD; YISSUM RESEARCH DEVELOPMENT COMPANY OF) 19 February 1998 (1998-02-19) page 1, line 3 - line 9 page 5, line 5 - line 9 ----- | 1-17 |
| X | DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 22 May 2002 (2002-05-22), WEN, B. ET AL: "Tyrphostin AG 1024 modulates radiosensitivity in human breast cancer cells" XP002977524 retrieved from STN Database accession no. 2002:141503 abstract & BRITISH JOURNAL OF CANCER , 85(12), 2017-2021 CODEN: BJCAAI; ISSN: 0007-0920, 2001, ----- | 1-17 |
| X | LEI W ET AL: "ENHANCEMENT OF CHEMOSENSITIVITY AND PROGRAMMED CELL DEATH BY TYROSINE KINASE INHIBITORS CORRELATES WITH EGFR EXPRESSION IN NON-SMALL CELL LUNG CANCER CELLS" ANTICANCER RESEARCH, HELENIC ANTICANCER INSTITUTE, ATHENS,, GR, vol. 19, no. 1A, 1989, pages 221-228, XP000929677 ISSN: 0250-7005 abstract ----- | 1-17 |
| X | BENINI S ET AL: "INHIBITION OF INSULIN-LIKE GROWTH FACTOR I RECEPTOR INCREASES THE ANTITUMOR ACTIVITY OF DOXORUBICIN AND VINCRISTINE AGAINST EWING'S SARCOMA CELLS" CLINICAL CANCER RESEARCH, THE ASSOCIATION, DENVER, NJ, US, vol. 7, no. 6, June 2001 (2001-06), pages 1790-1797, XP001187566 ISSN: 1078-0432 abstract ----- | 1-17 |
| | ----- -/-- | |

| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT | | |
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| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | BEECH DERRICK J ET AL: "Insulin-like growth factor-I receptor antagonism results in increased cytotoxicity of breast cancer cells to doxorubicin and taxol" ONCOLOGY REPORTS, vol. 8, no. 2, March 2001 (2001-03), pages 325-329, XP009047699 ISSN: 1021-335X abstract Discussion ----- | 1-17 |
| X | WO 95/20960 A (ARCH DEVELOPMENT CORPORATION; DANA-FARBER CANCER INSTITUTE; WEICHSELBA) 10 August 1995 (1995-08-10) page 19, line 23 - line 34; claim 12 ----- | 1-17 |
| X | WO 02/080987 A (PROGENICS PHARMACEUTICALS, INC; OLSON, WILLIAM, C; MADDON, PAUL, J; MA) 17 October 2002 (2002-10-17) abstract page 14, line 3 - line 7 page 16, line 21 - line 22 ----- | 1-17 |
| X | WO 01/87307 A (CELGENE CORP) 22 November 2001 (2001-11-22) page 16, line 22 - line 27 page 18, line 24 - line 25 ----- | 1-17 |
| X | WO 02/17904 A (GOVERNMENT OF MALAYSIA; MASSACHUSETTS INSTITUTE OF TECHNOLOGY; OH, SE-) 7 March 2002 (2002-03-07) page 3, line 15 - line 19 page 7, line 31 - page 8, line 3 page 10, line 17 - line 18 ----- | 1-17 |
| P,X | WO 2004/030627 A (BRISTOL-MYERS SQUIBB COMPANY; CARBONI, JOAN, M; HURLBURT, WARREN, W; G) 15 April 2004 (2004-04-15) abstract ----- | 1-17 |

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2005/005922

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-17

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-17

method of inhibiting tumour cell growth using a combination of a cytotoxic/chemotherapeutic agent and insulin like growth factor receptor-1 (IGF-1R) inhibitor

2. claims: 18-32

method of inhibiting tumour cell growth using a combination of a compound which lowers the concentration of insulin-like growth factor and insulin- like growth factor receptor-1 (IGF-1R) inhibitor

3. claims: 33-38

method of inhibiting tumour cell growth using a combination of an anti-diabetic agent and insulin-like growth factor receptor-1 (IGF-1R) inhibitor

4. claims: 39-53 part

method of inhibiting tumour cell growth using a compound which decreases the expression of insulin- like growth factor receptor-1 (IGF-1R) inhibitor

5. claims: 39-59 part

method of inhibiting tumour cell growth or reducing angiogenesis or inducing apoptosis in a cell using an inhibitor of the activity of insulin- like growth factor receptor-1 (IGF-1R) wherein the inhibitor is a small molecule tyrosine kinase inhibitor

6. claims: 39-59 part

method of inhibiting tumour cell growth or reducing angiogenesis or inducing apoptosis in a cell using an inhibitor of the activity of insulin- like growth factor receptor-1 (IGF-1R) wherein the inhibitor is an anti-IGF1R neutralizing antibody

7. claims: 39-59 part

FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

method of inhibiting tumour cell growth or reducing
angiogenesis or inducing apoptosis in a cell using an
inhibitor of the activity of insulin- like growth factor
receptor-1 (IGF-1R) wherein the inhibitor is the IGF-1R
antagonist JB-1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2005/005922

| Patent document cited in search report | | Publication date | Patent family member(s) | Publication date |
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INTEF \TIONAL SEARCH REPORT

Information on patent family members

Ir \tional Application No

PCT/US2005/005922

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